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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/083,413
Filing Date: February 27, 2002
Appellants: DOMB ET AL.

Patrea Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 19, 2006 appealing from the Office action mailed March 10, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appellants' statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellants' statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

A substantially correct copy of appealed claims 1-4, 6-17, 19-26 and 38 appears on pages 18-22 of the Appendix to the Appellants' brief. The minor errors are as follows:

In Claim 6, line 1, the word active should appear before the term "agent ".

In Claim 16, line 3, there is a space between "benzocaine" and "e", which appears to be no more than a minor typographical error.

In Claim 26, line 2, a strikethrough appears in the word lightly, that is "~~lightly~~", which appears to be a typographical error because the amendment to the claim filed on December 24, 2005 removed the term from the claim language of Claim 26, as well as the amendment to the claim filed on September 22, 2006.

(8) Evidence Relied Upon

US 4,772,470	INOUE et al.	9-1988
US 4,226,848	NAGAI et al.	10-1980
US 5,939,050	IYER et al.	8-1999
US 6,197,305	FRIEDMAN et al.	3-2001

Lawless, Julia. 1995. *The Illustrated Encyclopedia of Essential Oils: The Complete Guide to the Use of Oils in Aromatherapy and Herbalism*, USA: Element Books, pp. 115, 120, 123, 134, 139-141, 196 and 197.

George Odian. 1991. *Principles of Polymerization*, Third Edition, New York: John Wiley & Sons, pp. 520-521.

(9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claims 1-4, 6, 15-17, 22-24 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Inoue et al. (US 4,772,470).

Independent Claim 1 is directed to a solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising: (a) a therapeutically effective amount of at least one herbal active agent wherein the herbal active agent is

selected from the group consisting of bioactive herbs, herbal extracts, tinctures, essential oils, and mixtures thereof, and (b) a pharmaceutically acceptable solid bioadhesive carrier, comprising a mucoadhesive synthetic polycarboxylic acid polymer in an amount from about 40 to 99 percent based on the weight of the whole composition in a form suitable for administration and adhesion to the oral mucosa. Dependent claims are directed to a solid composition wherein the composition is in the form of a disc of 2 to 15 mm diameter and 0.4 to 2.3 mm thick that adheres to the oral mucosal for at least 30 minutes; and, wherein the composition is in the form of a disc 5 to 11 mm in diameter and 1 to 2 mm thick with tissue adherence of at least 1 hour; wherein the herbal active agent is selected from the group consisting of anti-inflammatory, analgesic, antiaching, anesthetic, antimicrobial, antifungal, antiseptic, antiviral, antibiotic, antiparasite agents, and combinations thereof; and, wherein the herbal agent is selected from the group consisting of Echinacea, Salvia officinalis, Hypericum, Myrrh, Camphoria, Uncaria, menthol, Plantago, Baptisia, Calendula, Phytolacca, Catechu black, Coneflower, Krameria, Tsuga, grape fruit seed extract, Rosmarinus, Styrax, Crataegus, Glycerrhiza, Angelica, Kramerica, Matricaria, Mallow, Propolis, Sage, berberine from Hydrastis canadensis L., plant family Berberidaceae, gentian from the Gentianaceae family of plants for the treatment of fungal infections, monoterpenes of three unsaturations, Taraxacum extract, Lonicera flower extract, Scutellaria root extract, Gardenia fruit extract, Pulsatilla root extract, Pueraria root extract, Radix Gentianae Longdancao antifungal extract, and combinations thereof. Dependent claims are further directed to a composition further comprising a non-herbal active agent; and, wherein the

non-herbal active agent is selected from the group consisting of at least one base or acid-addition salt of procaine, lidocaine, prilocaine, meprivacaine, dyclonine, dibucaine, benzocaine, chloroprocaine, tetracaine, bupivacaine, and etidocaine; and, wherein the non-herbal active agent is selected from the group consisting of at least one base or acid-addition salt of dexamethasone, triameinolone, hydrocortisone, amphotericine B, nystatin, itraconazole, chlorhexidine, quaternary ammonium salts, parabens, and dextranase enzymes. Dependent clams are directed to a composition wherein the solid bioadhesive carrier is selected from the group of a crosslinked synthetic polycarboxylic acid polymer and mixtures thereof; and, wherein the polymer is a copolymer of one or more polymers selected from the group consisting of hydroxypropyl cellulose, hydroxypropyl methycellulose, hydroxyethylcellulose, carboxymethyl cellulose, dextran, arabinogalactan, pullulan, guar-gum, hyaluronic acid, pectins, starch derivatives, acrylic acid polymers, polymer of acrylic acid esters, polymers of vinyl alcohols, alkoxy polymers, polyethylene oxide polymers, polyethers and combinations thereof; and, further comprising an excipient selected from the group consisting of fillers, tableting excipients, lubricants, enhancers, flavors, taste-masking agents, pH controlling compounds, dyes, stabilizers, enzyme inhibitors, and mixtures thereof. Dependent claims are further directed to a composition wherein the solid bioadhesive carrier is selected from polyacrylic acid polymers [~~lightly~~] crosslinked with a polymer selected from the group consisting of polyalkenyl polyether, carboxymethylcellulose, hydroxymethylcellulose, and mixtures thereof. Dependent claims are further directed to

a composition, wherein the composition has a surface area ranging from about 0.4 to about 3 cm^2.

Inoue teaches a solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising a therapeutically effective amount of a drug and a mixture of polymers of polycarboxylic acid and/or a polycarboxylic acid anhydride and a vinyl acetate polymer that adheres to the oral mucosa. The amount of the polycarboxylic acid polymer comprising the referenced composition is an amount from about 40% or greater than 40% based on the weight of the whole composition. Drugs incorporated into the making of the Inoue' composition include bioactive herbals or extracts thereof (for example, glycyrrhizin, hinokitiol, menthol, tannin, berberine, *etc.*); steroids, vitamins; anti-inflammatories (for example, glycyrrhizin, an extract of *Glycerrhiza*, *etc.*); enzymes; and non-herbal active agents (for example, mepivacaine, tetracaine, dibucaine and dexamethasone). Excipients, such as dyes and flavoring matters, may further comprise the Inoue' composition. *See* Column 10, lines 5-14. In Column 8, lines 45-61, Inoue teaches that the referenced composition has a thickness from 10 to 150 μm; a width ranging from 7 to 15mm; and, a diameter ranging from 5 mm to 20 mm. In Column 11, lines 3-10, Inoue teaches that the residency time of the compositions in oral mucosal tissue is generally 3 to 4 hours. In Column 14, lines 49-62, Inoue teaches a composition wherein the bioadhesive carrier comprises polyvinyl acetate, diisopropanolamine and a carboxyvinyl; and a therapeutic effective amount of *Lithospermi* Radix extract, which is in the form of a disc and having a diameter of 10mm.

Claims 1-3, 15-17, 22-24, 26 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nagai et al. (US 4,226,848).

Nagai teaches a solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising: (a) a therapeutically effective amount of a drug (for example, anti-inflammatory agents, fungicides, anesthetics, the enzymes lysozyme hydrochloride and dextranase, chlorohexidine, quaternary ammonium salts, hydrocortisone, vitamins and benzocaine, as set forth in Column 5, line 57 to Column 6, line 17) and; (b) about 50 to about 95% by weight of a cellulose ether (*See* Column 4, lines 46-68.) and about 50 to about 5% of a homo- or copolymer of carboxylic acid, such as a polycarboxylic acid (*See* Column 5, lines 18-21.). Excipients, which may further comprise the composition taught by Nagai include fillers, tableting agents, lubricants, flavors, taste-masking agents. *See* Column 6, lines 24-39. In Column 7, lines 2-11, Nagai teaches that the referenced composition has a residency time for 4 hours in the oral mucosal cavity. In Column 18, lines 23-44, Nagai teaches discs having a thickness of 1.4 mm and a diameter having a thickness of 10.0 mm comprising 50% of a polycarboxylic copolymer (Carbopol 934) and 50% of hydroproxycellulose and triamcinolone acetonide.

The reference anticipates the claimed subject matter.

Claims 1-4, 6-12, 15-17, 19, 22-24 and 38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Inoue et al. (US 4,772,470) in view of Iyer et al. (US

5,939,050) and Friedman et al. (US 6,197,305) with evidence provided by Lawless (1995).

Dependent claims recite a composition wherein the herbal active agent is an essential oil selected from the group of citronella oil, lemon oil, citron oil, pomelo peel oil, cedarwood oil, juniper berries oil, lemon basil oil, Rosmarinus officinalis oil, cinnamon oil, cajeput oil, eucalyptus oil, fennel oil, geranium oil, girofle oil, lavender oil, clove oil, spearmint oil, myrtle oil, oregano oil, pine oil, rosemary oil, sarriette oil, thyme oil, tea-tree oil, and combinations thereof; wherein the herbal active agent is and essential oil selected from the group consisting of cinnamon oil, tea-tree oil, citronella oil, and combinations thereof; wherein the herbal active agent comprises at least one monoterpene with three unsaturations; wherein the herbal active agent is an essential oil and the essential oil is a natural or synthetic mixture consisting of limonene and at least one myrcene, a-pinene, b-pinene and sabinene characterized in that at least 60% by weight of the mixture is limonene; wherein the monoterpene with three unsaturations is a citrus oil selected from the group consisting of lemon oil, pomelo oil, citron oil, and combinations thereof; further comprising a salt selected from the group consisting of $MgBr_2$, NaCl, KCl, and mixtures thereof.

The teachings of Inoue are set forth above. Inoue teaches the instantly claimed composition except for wherein the herbal active agent is an essential oil; wherein the herbal active agent of claim 6 comprises at least one monoterpene with three saturations, wherein the essential oil is a natural or synthetic mixture consisting of myrcene, a-pinene, b-pinene, and sabinene characterized in that at least 60% by weight

of the mixture is limonene, and wherein said monoterpenes with three unsaturations is of citrus oil selected from the group consisting of lemon, pomelo and citron; and wherein the composition further comprises a salt selected from the group consisting of $MgBr_2$, NaCl, KCl, and mixtures thereof . However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add the instantly claimed ingredients to the composition taught by Inoue to provide the instantly claimed invention because at the time the invention was made it was known in the art that the claim-designated agents were useful in the making of topical compositions for the treatment of oral mucosal tissue, as evidenced by the teachings of Iyer and Friedman. Firstly, Iyer teaches various herbal active agents, such as essential plant oils and herbal extracts have antimicrobial activity that are useful as therapeutic agents such as in oral hygiene products. For example, Iyer teaches antimicrobial compositions comprising at least two antimicrobial agents, agent A and agent B, which exhibit reduce MIC values relative to the MIC for the agents making up the combination measured alone. For example, in Column 3, lines 11-26, Iyer teaches that agent A and agent B are selected from the group consisting of berberine, cedarwood oil, chloramphenicol, citral, citronella oil, cocamidopropyl dimethylglycine, *Glycyrrhiza glabra* extract, hinokitol, juicy fruit basil oil, juniper berries oil, lemon basil oil, lemon oil, and *Rosmarinus officinalis* oil. Secondly, Friedman teaches a combination of an herbal extract and an essential oil which exerts prolonged antifungal activity on mucosal membranes. The herbal extracts include material selected from the group consisting of Plantago, Hypericum, Echinacea, Baptisia, Calendula, Myrrh, Phytolocca, Salvia, Catechu black, Coneflower, Krameria,

Tsuga, Rosmarinus, Styrax, Crataegus, Glycerrhiza, Angelica, Krameria, Matricaria, Mallow, Propolis (beehive material), and Sage; and the essential oils are selected from cinnamon oil, cajeput oil, citronella oil, eucalyptus oil, fennel oil, geranium oil, lavender oil, lemon oil, spearmint oil, myrte oil, oregano oil, pine oil, rosemary oil, sarriette oil, thyme oil, and tea-tree oil (see Column 1, lines 6-10; Column 2, lines 38-59; and claims). In Column 5, lines 9-39, Friedman further teaches that the herbal extracts are in the form of a tincture of botanical materials. In Figures 1 and 2, Friedman shows that the referenced compositions have prolonged activity against *Aspergillus niger* and *Candida albicans*. In Column 4, lines 18-37, Friedman teaches that the compositions can be used to combat fungal infection of mucosal organs and the oral cavity. At the time the invention was made, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to add the instantly claimed ingredients to the composition taught by Inoue to provide the claimed invention because Iyer, like Inoue teaches that the active agents of his invention can be used in the making of therapeutic oral hygiene products for the treatment of stomatitis, as well as for growth control of bacteria, such as *Actinomyces viscosus, Campylobacter rectus, Fusobacterium nucleatum, Porphyromonas gingivalis, Streptococcus mutans* and *Streptococcus mutans* (see Column 3, lines 28-38 and 47-51 ; and Friedman teaches that the compositions of his invention have strong antibacterial activity and anti-inflammatory activity, as well as antifungal activity, which can be used in the making of oral products, and which can be used in the treatment of disease conditions such as *Herpes zoster* and *Herpes simplex* infections, dental ulcers, stomatitis, aphthous ulcers,

and abscesses (see Column 4, lines 31-37; Column 8, lines 36-42; Column 9, lines 66-67 to Column 10, lines 1-4; and Column 10, lines 30-51). One of ordinary skill in the art at the time the invention was made would have been further motivated and one would have had a high expectation of success to add the antimicrobial compositions taught by Iyer to the bioadhesive composition taught by Inoue to provide the claimed invention because Iyer teaches in Table 14 that the combination of the essential oil of lemon (which comprises 70% limonene, myrcene, pinenes and sabinene, as evidenced by the teaching of Lawless) in combination with an antimicrobial Agent B results in a significant decrease in the MIC value against various microorganisms which cause oral or periodontal disease. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add any of the claimed ingredients in the making of the claimed methods because it is well known that its *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten,* 459 F. 2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi,* 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

As each of the references clearly indicate that the various proportions and amounts of the ingredients used in the claimed composition or the claimed composition/pharmaceutical combinations are result variables, they would have been

routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by that reference.

According, the claimed the invention was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

(10) Response to Argument

With regard to the rejection of Claims 1-4, 6, 15-17, 22-24 and 38 made under 35 U.S.C. § 102(b) as being anticipated by Inoue et al. (US 4,772,470), Appellants argue case law. Appellants' main argument is directed to the idea that Claim 1 is novel over the teachings of Inoue because Inoue does not disclose a composition comprising a bioadhesive carrier in an amount from about 40 to 99 percent based on the weight of the whole composition. Appellants further argue that no information is given regarding the weight of the support film, thus the weight percent of the bioadhesive material cannot be determined. Appellant concludes that Inoue does not disclose each and every element of Claim 1; and, thereby neither Claim 1 nor claims dependent thereon are anticipated by the teachings of Inoue.

Appellants' arguments have been fully considered but found unpersuasive because Inoue expressly teaches, "The amount of these topical drugs to be incorporated in the oral preparation varies depending on the kind thereof, but from considerations of pharmacological effects and adhesion to the mucous membrane, it usually ranges from 0.0001 to 35% by weight, and preferably from 0.0002 to 20% by weight, based on the preparation. When positive administration of the drug to the oral

mucosa is expected, the drug is preferably present in the adhesive film side. In the treatment of bad breath and the like, it may be present in the support side." *See* Column 9, lines 54-63. Since Inoue clearly teaches incorporating topical drugs into the prior art composition in an amount of 0.0001 to 35% by weight based on the oral preparation, and preferably from 0.0002 to 20% by weight based on the preparation, the remaining weight portion of the prior art composition comprising the bioadhesive mucoadhesive carrier is deemed to be in an amount encompassed by about 40 to 99 percent based on the weight of the whole composition, as instantly claimed by Appellant.

Secondly, Appellants argue that the compositions described by Inoue are films. Appellants further argue that Inoue does not disclose or suggest disks prepared by compression molding having the diameters and thickness specified in claims 2 and 3. Appellants further argue that Inoue does not disclose or suggest a composition wherein the surface area is from about 0.4 to 3 cm^2. Appellants' arguments have been fully considered but found neither persuasive nor commensurate in scope to the limitations of the instantly claimed invention. Appellants' arguments are not commensurate in scope to the limitations of the instantly claimed invention because nowhere in the claims do Appellants direct the claimed invention to a solid, self-bioadhesive composition for topical application prepared by compression molding. Appellants' arguments are not persuasive because the prior art composition taught by Inoue has a thickness of at least 5 μm, which encompasses larger thicknesses such as 400 μm (0.4 mm), as instantly claimed by Appellants. *See* patent claim 1. Moreover, Inoue teaches that the

referenced composition has a width ranging from 7 to 15 mm; and, a diameter ranging from 5 mm to 20 mm, in Column 8, lines 45-61. Inoue also teaches that the residency time of the compositions in oral mucosal tissue is generally 3 to 4 hours which reads on at least 1 hour, in Column 11, lines 3-10.

Thirdly, with particular regard to Claims 22 and 26, Appellants make the new argument that there is no disclosure in Inoue that the polymers comprising the referenced composition are cross-linked. Appellant's argument has been fully considered but not found persuasive. It is noted that the Inoue teaches use of polycarboxylic acid polymers and copolymers containing 20% or more carboxylic acid groups, in Column 4, lines 6-27. These polymers are neutralized using polyvalent metal salts, such as the oxides of zinc, calcium, magnesium, and the like. *See* Column, lines 41-65. This neutralization with polyvalent metal salts would be understood by the skilled artisan to inherently cause cross-linking of the polymer. Thus, the neutralization of the polycarboxylic acids used in the making of the composition taught by Inoue inherently results in cross-linking of the polymers. Only for the purpose of rebutting Appellants' argument, the teachings of Odian are relied upon herein to support the Examiner's position that the cross-linking is inherent to the processing of the Inoue' polycarboxylic acid polymers. The Odian reference is an excerpt from a polymer chemistry textbook; and, thus the teachings thereof would be well known to a person of ordinary skill in the art. Odian teaches that when polymers of 5 –10% acrylic and methacrylic acid (that is, polycarboxylic acids with 5 –10% carboxylic acid functional groups) are neutralized with oxides of zinc, magnesium, and aluminum, *etc.*, the

polymers become cross-linked. Since the cross-linking reaction, as taught by Odian, occurs when the reactive acid group is present in only 5 –10% concentrations, the artisan would immediately recognize that cross-linking would be even more prevalent in the Inoue' patent, since the polymers thereof contain 20% or more carboxylic acid. It is noted that the reactive moiety in the cross-linking reaction is the carboxylic acid group. Given the foregoing, Claims 22 and 26 are anticipated by the teaching of Inoue *inter alia* because Inoue teaches polycarboxylic acid polymers that are inherently cross-linked.

The reference teaches the claimed subject matter.

With regard to rejection of Claims 1-3, 15-17, 22-24, 26 and 38 made under 35 U.S.C. 102(b) as being anticipated by Nagai et al. (US 4,226,848), Appellants argue that the claimed invention is novel over the teachings of Nagai because none of the drugs comprising the prior art composition are bioactive herbs, herbal extracts, tinctures, essential oils, and/or mixtures thereof as required by Claim 1. Appellants' argument has been fully considered. However, Appellants' argument is not found persuasive because Nagai teaches a solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising: (a) a therapeutically effective amount of a bioactive herbal agent, as well as non-herbal active agents (for example, non-herbal active agents include anti-inflammatory agents, fungicides, anesthetics, the enzymes lysozyme hydrochloride and dextranase, chlorohexidine, quaternary ammonium salts, hydrocortisone, vitamins and benzocaine, as taught in Column 5, line 57 to Column 6, line 17; and herbal active agents include colchicines, an

alkaloid obtained from plants of the genus *Colchicum*; digitalis and digoxin obtained from plants of the genus *Digitalis*; and papaverine hydrochloride and codeine phosphate obtained from plants of the genus *Papaver*, as taught in C0lumn 5, line 58 to Column 6, line 17) and; (b) about 50 to about 95% by weight of a cellulose ether (*See* Column 4, lines 46-68.) and about 50 to about 5% of a homo- or copolymer of carboxylic acid, such as a polycarboxylic acid (*See* Column 5, lines 18-21.). Excipients, which may further comprise the composition taught by Nagai include fillers, tableting agents, lubricants, flavors, taste-masking agents. *See* Column 6, lines 24-39. In Column 7, lines 2-11, Nagai teaches that the referenced composition has a residency time for 4 hours in the oral mucosal cavity.

Appellants also argue that the compositions described in Nagai contain 50 to 95% by weight of cellulose ether and 50% to 5% of a homo- or copolymer of acrylic acid or a pharmaceutically acceptable thereof. Appellants further argue that there is no disclosure that the polymers are cross-linked. Appellants' arguments have been thoroughly considered. However, Appellants' arguments are not persuasive because Nagai teaches discs having a thickness of 1.4 mm and a diameter having a thickness of 10.0 mm comprising 50% of a polycarboxylic copolymer (Carbopol 934) and 50% of hydropropylcellulose and triamcinolone acetonide, in Column 18, lines 23-44. One of ordinary skill in the art would recognize that Carbopol 934 is a cross-linked carboxyvinyl-polymer (or in other words, a cross-linked polyacrylate polymer).

The reference teaches the claimed subject matter.

With regard to the rejection of Claims 1-4, 6-12, 15-17, 19, 22-24 and 38 under 35 U.S.C. 103(a) as being unpatentable over Inoue et al. (US 4,772,470) in view of Iyer et al. (US 5,939,050) and Friedman et al. (US 6,197,305) with evidence provided by Lawless (1995), Appellants argue case law.

In response to Appellants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to Appellants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the primary reference of Inoue was relied upon for the reasons set forth above. Since Inoue taught the instantly claimed invention except for the instantly claimed ingredients recited in the Markush groups of each of Claims 7-15 and 19, the secondary references of Iyer, Friedman and Lawless were relied upon because at the time the invention was made it was known in the art that the claim-designated agents were useful in the making of topical compositions for the treatment of oral mucosal tissue, as evidenced by the

teachings of Iyer and Friedman; and because Iyer taught in Table 14 that the combination of the essential oil of lemon (which comprises 70% limonene, myrcene, pinenes and sabinene, as evidenced by the teaching of Lawless) in combination with an antimicrobial Agent B results in a significant decrease in the MIC value against various microorganisms which cause oral or periodontal disease.

Thus, with Inoue providing the motivation to use a solid, self-bioadhesive composition as a topical application that adheres to oral mucosal that comprises a therapeutically effective amount of at least one herbal active agent, and a pharmaceutically acceptable bioadhesive carrier in an amount from about 40 to 90 percent based on the weight of the whole composition, and with Iyer suggesting the use of plant essential oils as therapeutic agents for use in oral hygiene products, and finally with Friedman teaching that combining an herbal extract and an essential oil with a sodium salt exerts a prolonged antifungal activity on mucosal membranes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the instantly claimed old and well-known ingredients to provide a composition for the use as a composition for application to a mucous membrane as suggested by the cited references. As each of the references clearly indicate that the various proportions and amounts of the ingredients used in the claimed composition or the claimed composition/pharmaceutical combinations are result effective variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by that reference. Therefore, the invention as a whole was clearly *prima facie* obvious in the absence to the contrary.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Michele C. Flood

Primary Examiner

Art Unit 1655

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